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I-GF-1 Signalling Controls the Hair Growth Cycle and the Differentiation of Hair Shafts

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TO THE EDITOR

We read with interest the article entitled ''IGF-1 signalling controls the hair growth cycle and the differentiation of hair shafts'' (Weger and Schlake, 2005).

Recently, we have reported documentation of the role of primary IGF-1 deficiency on hair structure in human beings (Lurie *et al.*, 2004). Laron syndrome is a recessively inherited disease of primary IGF-1 deficiency owing to primary growth hormone insensitivity. Affected children have sparse hair growth and frontal recessions. The hair is thin and easy to pluck, and young adults have various degrees of alopecia. Despite signs of early aging, graying of the hair is delayed and reduced (Laron, 2004). The syndrome is caused by deletions or mutations in the growth hormone receptor or postreceptor pathways, which lead to an inability to generate IGF-1 (Laron, 2002, 2004). We investigated the effect of primary IGF-1 deficiency on hair structure by sampling the hair of 11 patients with Laron syndrome. The most significant structured defect, pili torti et canaliculi, was found in two young, untreated patients. Grooving, tapered hair, and trichorrhexis nodosa were found in the remainder. IGF-1-treated patients had either none or significantly fewer pathological changes compared to the untreated patients.

We believe our report (Lurie *et al.*, 2004) supplements that of Weger and Schlake (2005) in demonstrating the regulatory function of IGF-1 on hair growth in man from a different direction.

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Response to Ben Amitai *et al.*

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Whereas IGF-I has been initially described as a potent mitogen supporting cell growth and survival (Stewart and Rotwein, 1996), there is accumulating evidence for its participation in diverse differentiation processes (Musaro and Rosenthal, 1999; Hsieh *et al.*, 2004). Our recent work on IGF-I confirmed this dual role for the murine hair follicle (Weger and Schlake, 2005a, b). In man, an IGF-I deficiency is associated with Laron syndrome (Laron, 2002). Interestingly, patients show impaired hair production and structural abnormalities of hair shafts (Lurie *et al.*, 2004). On the molecular level, people with Laron syndrome are similar to Ivl::Igfbp3 mice that are supposed to have reduced levels of freely available IGF-I. The suppression of endogenous signalling in these mice causes a remarkable thinning of hair shafts that has been also described for Laron syndrome (Lurie *et al.*, 2004; Weger and Schlake, 2005b); by contrast, overexpression of *Igf-I* appeared to increase murine hair thickness (Weger and Schlake, 2005a). However, other structural defects of hair shafts were only observed in Ivl::Igf-I mice (Weger and Schlake, 2005a); Ivl::Igfbp3 hair shafts looked fairly normal as opposed to hair from Laron syndrome patients (Lurie *et al.*, 2004; Weger and Schlake, 2005b). This discrepancy between man and mouse might be owing to several reasons: firstly, it may point to a fundamental difference between these species. Actually, there is already precedence for structural diversity; whereas the murine hair shaft medulla forms easily visible air spaces during differentiation, they are lacking in human hair. Secondly, it is possible that the obtained suppression of IGF-I signalling in Ivl::Igfbp3 mice is lower than in people suffering from Laron syndrome. However, data on mouse lines with significantly different expression levels of *Igfbp3* suggest that effects are restricted to quantitative alterations of

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